present study was a farmer or hunter, but most owned, or formerly kept, dogs or cats, and these could be a possible risk-factor for this infection [15,16]. Overall, the results of this study suggest that clinicians and health authorities in Slovenia should give greater attention to AE in the future.

ACKNOWLEDGEMENTS

This work was supported by Grant no. P3-0083 from the Ministry of Higher Education, Science and Technology of the Republic of Slovenia.

REFERENCES

1. Craig P. *Echinococcus multilocularis*. *Curr Opin Infect Dis* 2003; **16**: 437–444.
2. Romig T. Epidemiology of echinococcosis. *Lagenbecks Arch Surg* 2003; **388**: 209–217.
3. Auer H, Aspöck H. Echinococcosis in Austria. *Zentralbl Bakteriol* 1990; **272**: 498–508.
4. McManus DP, Zhang W, Li J, Bartley PB. Echinococcosis. *Lancet* 2003; **362**: 1295–1304.
5. Ekert J, Deplazes P. Biological, epidemiological, and clinical aspect of echinococcosis, a zoonosis of increasing concern. *Clin Microbiol Rev* 2004; **17**: 107–135.
6. Jenkins DJ, Romig T, Thompson RCA. Emergence/re-emergence of *Echinococcus* spp.—a global update. *Int J Parasitol* 2005; **35**: 1205–1219.
7. Liance M, Janin V, Bresson-Hadni S, Vuitton DA, Houin R, Piarroux R. Immunodiagnosis of echinococcosis: confirmatory testing and species differentiation by a new commercial Western blot. *J Clin Microbiol* 2000; **38**: 3718–3721.
8. Eckert J, Deplazes P. Alveolar echinococcosis in humans: the current situation in Central Europe and the need for countermeasures. *Parasitol Today* 1999; **15**: 315–319.
9. Gloor S, Bontadina F, Hegglin D, Deplazes P, Breitenmoser U. The rise of urban fox population in Switzerland. *Mamm Biol* 2001; **66**: 155–164.
10. Torgerson PR, Budke CM. Echinococcosis—an international public health challenge. *Res Vet Sci* 2003; **74**: 191–202.
11. Kern P, Bardonnet K, Renner E *et al*. European echinococcosis registry: human alveolar echinococcosis, Europe, 1982–2000. *Emerg Infect Dis* 2003; **9**: 343–349.
12. Kern P, Ammon A, Kron M *et al*. Risk factors for alveolar echinococcosis in humans. *Emerg Infect Dis* 2004; **10**: 2088–2093.
13. Brglez J. Echinococcosis in Slovenia. *Zdrav Vestn* 1970; **39**: 265–267.
14. Brglez J, Kryštufek B. Metacestode of *Echinococcus multilocularis* in *Apodemus flavicollis* in Slovenia. *Zb Biotehn Fak Vet* 1984; **21**: 173–176.
15. Macpherson CNL. Human behaviour and epidemiology of parasitic zoonoses. *Int J Parasitol* 2005; **35**: 1319–1331.
16. Romig T, Thoma D, Weible AK. *Echinococcus multilocularis*—a zoonosis of anthropogenic environments? *J Helminthol* 2006; **80**: 207–212.

RESEARCH NOTE

Paediatric varicella hospitalisations in France: a nationwide survey

E. Grimprel[1,2], C. Levy[1,3], F. de La Rocque[1,3], R. Cohen[1,3], B. Soubeyrand[4], E. Caulin[4], T. Derrough[4], A. Lecuyer[3], P. d'Athis[5], J. Gaudelus[1] and the Pediatricians Working Group[1]

[1]Groupe de Pathologie Infectieuse Pédiatrique de la Société Française de Pédiatrie (GPIP), [2]Service de Pédiatrie Hôpital Trousseau, Paris, [3]Association Clinique et Thérapeutique Infantile du Val de Marne (ACTIV), [4]Laboratoire Sanofi Pasteur MSD and [5]Département de Biostatistique, Centre Hospitalier Universitaire Dijon, Dijon, France

ABSTRACT

Paediatric patients hospitalised with varicella (n = 1575) were reported to a French national network between March 2003 and July 2005. Superinfection was identified in 50.3% of cases, principally of skin and soft-tissue (36.5%). The risk of superinfection increased with fever relapse, use of non-steroidal anti-inflammatory drugs, prolonged fever, an age of 1–5 years, and contamination at the childminder's home. Neurological complications were observed in 7.8% of cases, while pulmonary complications were less frequent (3.1%). Forty-nine patients had sequelae and eight patients died. Surveillance should continue in France with a view to the future implementation of a universal vaccination programme.

Keywords Complications, paediatric patients, risk-factors, superinfection, surveillance, varicella

Original Submission: 25 July 2006; **Revised Submission:** 11 December 2006; **Accepted:** 19 December 2006

Clin Microbiol Infect 2007; **13**: 546–549
10.1111/j.1469-0691.2007.01706.x

Varicella is a mild infectious disease preventable by vaccination [1,2]. Only high-risk individuals are

Corresponding author and reprint requests: E. Grimprel, Service de Pédiatrie, Hôpital Armand Trousseau, 26 Avenue du Dr Arnold Netter, F75012 Paris, France
E-mail: emmanuel.grimprel@trs.ap-hop-paris.fr

currently targeted for varicella vaccination in France, and 700 000 cases of varicella are diagnosed annually (estimated incidence 1420/100 000), with 90% occurring in children aged <10 years [3] (http://rhone.b3e.jussieu.fr/senti/docs/bilans/2004/BilanRS_2004–050314V15.pdf 2004). Complications are reported in 8–9% of cases, with 15–25 deaths each year, mainly in adults and the elderly [4,5]. In total, 3500 patients are hospitalised each year with a diagnosis of varicella (with 75% aged <15 years), but only 33% are recorded as having complications [4]. However, complications are the primary cause of varicella-related hospitalisations according to regional French paediatric studies [6,7]. In order to better estimate the burden of paediatric hospitalisations caused by varicella in France, a national surveillance network was established. The present report presents a descriptive analysis of the results of surveillance for the first 2 years.

In total, 200 paediatric wards in hospitals located throughout France participated in the study. Each patient admitted for ongoing varicella and/or complications or events attributed to varicella was recorded. Hospitalisations unrelated to varicella, and conditions with an onset of varicella >5 days after admission, were excluded. For each case, a standard form recording age, gender, underlying conditions, reason for admission, source of infection, nature and type of any varicella-associated complications, and outcome was completed by a designated clinical investigator.

Data were analysed using Statview II (Abacus Concepts, Cary, NC, USA) and Stata 8 (StataCorp, College Station, TX, USA) software to compare frequencies, perform chi-square tests and conduct bivariate and multivariate analyses. The contribution of selected factors, e.g., age, gender, source of varicella-zoster virus infection, use of non-steroidal anti-inflammatory drugs, corticosteroid therapy, immunodeficiency, and severity of varicella infection (extensive and/or haemorrhagic), as factors potentially related to superinfection, was analysed by logistic regression models.

Overall, 165 paediatric wards contributed at least one case report form between March 2003 and July 2005, describing a total of 1575 cases, including 38 (2.4%) that required intensive care. The median age of the patients was 2.0 years; 87.5% were aged <5 years, and 2.7% were neonates. The male:female ratio was 1:1.25. The majority (73.7%) of cases occurred in the spring and early summer months, with a peak in June (18.8%) and a nadir in September (1.0%). The mean length of hospitalisation was 5 (median 4.0 ± 3.7) days. The source of varicella-zoster virus infection was identified for 56.1% of cases, of which the patient's household accounted for 64%, a day care centre/school for 27.5%, and a childminder's home for 4.9%.

In 41.8% of cases, the following risk-factors for severe or complicated varicella were identified: corticosteroid therapy (106 cases, 8.3%); systemic therapy (40 cases, 3.1%); topical therapy (39 cases, 3.1%); and inhaled therapy (39 cases, 3.1%). Forty-two (2.7%) children were aged <1 month, 20 (1.3%) had received immunosuppressant chemotherapy, and four (0.3%) were infected

Table 1. Complications and other potential reasons for hospitalisation with varicella infection

Identified complication	*n* (%)[b]
Superinfections[a]	792 (50.3)
Skin/soft-tissue infection	575 (36.5)
Cellulitis	390 (24.8)
Abscess	114 (7.2)
Necrotising skin lesion	73 (4.6)
Scalded skin syndrome	44 (2.8)
Necrotising fasciitis	13 (0.8)
Other localisations	198 (12.6)
Bacterial pneumonia	49 (3.1)
Ear, nose and throat	45 (2.9)
Bacteraemia	34 (2.2)
Lower respiratory tract infections	28 (1.8)
Arthritis	22 (1.4)
Shock	11 (0.7)
Pleurisy	10 (0.6)
Other infections	10 (0.6)
Osteomyelitis	9 (0.6)
Bacterial meningitis	3 (0.2)
Neurological complications	127 (8.1)
Cerebellitis	83 (5.3)
Encephalitis	25 (1.6)
Other neurological complications	15 (1.0)
Aseptic meningitis	11 (0.7)
Neuritis	6 (0.4)
Cerebral vascular thrombosis	1 (0.06)
Pulmonary complications	49 (3.1)
Varicella pneumonia	38 (2.4)
Acute respiratory distress syndrome	11 (0.7)
Haematological complications	30 (1.9)
Thrombocytopenic purpura	19 (1.2)
Other haematological complications	5 (0.3)
Disseminated intravascular coagulopathy	4 (0.3)
Haemorrhagic syndrome	3 (0.2)
Other complications	141 (9.0)
Febrile seizure	116 (7.4)
Hepatitis	19 (1.2)
Arthritis	5 (0.3)
Inappropriate anti-diuretic hormone syndrome	3 (0.2)
Other reasons for hospitalisation	
Fever	1042 (66.2)
Risk-factor or underlying condition	659 (41.8)
Severity of infection	344 (21.8)
Digestive problems	200 (12.7)
Social considerations	73 (4.6)
Intercurrent disease	59 (3.7)

[a]Presumed or confirmed.
[b]Reasons for hospitalisation are not exclusive and percentages do not add up to 100%.

with human immunodeficiency virus. Other conditions, i.e., atopic dermatitis (with or without local steroid treatment), underlying disease and recent non-steroidal anti-inflammatory drug use (ibuprofen and/or acetylsalicylic acid), were associated with 10%, 4.1% and 18% of cases, respectively.

The main reason for hospitalisation was the occurrence of a complication (76.2%; Table 1).

Bacterial superinfections were the most frequent type of complication (792 cases, 50.3%), mainly involving skin and soft-tissue (36.5%); these were more prevalent (82.1%) in children aged <5 years (mean age 2.1 ± 1.7 years, median age 2.0 years). Using a multiple regression analysis model, the risk of superinfection increased with fever relapse (OR 3.06, 95% CI 1.5–6.4), non-steroidal anti-inflammatory drug use (OR 2.65, 95% CI 1.8–3.4), prolonged fever (OR 2.25, 95% CI 1.5–3.3), an age of 1–5 years (OR 2.25, 95% CI 1.4–3.8), contamination at the childminder's home (OR 2.13, 95% CI 1.0–4.4) and an age of <1 year (OR 1.72, 95% CI 1.0–2.9). A bacterial agent was identified in 299 (37.8%) superinfections (Table 2). The two pathogens isolated most frequently were *Staphylococcus aureus* (n = 176) and group A β-haemolytic streptococci (n = 113). Both of these pathogens could be invasive, and they were isolated from blood in 24 cases each. Other pathogens, e.g., *Streptococcus pneumoniae* (n = 11), were identified mainly in respiratory superinfections. *Neisseria meningitidis* was identified in three cases of bacterial meningitis. Neurological complications (excluding febrile seizure) occurred more frequently in older children (mean age 4.0 ± 3 years, median 3.0 years), and represented the most frequent complication (19.6%) in individuals aged >6 years.

The outcome was favourable in most cases, with sequelae recorded for only 49 patients; these sequelae were mostly cutaneous (44 scars) and neurological (n = 5), but eight patients died. All but one (nephrotic syndrome) of the eight patients who died were considered to be immunocompetent before admission. Most died during a fever or a sudden shock event shortly after admission, suggesting a septic or toxic mechanism.

This study is one of the largest studies of varicella-associated hospitalisations, and is the largest study carried out in Europe to date. Hospitalisation for varicella and varicella-associated complications was justified by valid medical reasons in most cases. In the present study, varicella-associated complications were frequent, with most occurring in children without any identified risk-factors. Most complications were superinfections, with a predominance of skin and soft-tissue localisations. As reported previously, *Staph. aureus* and group A β-haemolytic streptococci are the predominant agents responsible for

Table 2. Pathogenic agents and infectious complications associated with varicella infection

	No. of cases		*Staphylococcus aureus*		GABHS		GABHS + *Staph. aureus*		Other	
	Total	Pathogen identified	No. of infections[a]	No. of invasive infections[a]	No. of infections	No.of invasive infections[a]	No. of infections	No. of invasive infections[a]	No. of infections	No. of invasive infections[a]
Cellulitis	390	161	91	6(bl)	54	5(bl)	11	1(bl)	2 *Staph. epid.* 1 Hi 1 Sp + Hi 1 SA + Hi + MC	0 0 0
Abscess	114	44	19	1(af)	23	3(bl) + 1(af)	1	0	1 SA + Hi + MC	0
Necrotising skin lesion	73	27	22	3(bl)	3	2(bl) + 1(pl)	1	0	1 *Strep. fugines*	0
Scalded skin syndrome	44	26	23	0	1	0	1	1(bl)	1 *Staph. epid.*	0
Necrotising fasciitis	13	10	3	0	7	1(bl)	0		0	
Arthritis	22	14	5	2(bl) + 1(af)	8	3(bl) + 3(af)	0		1 *Kingella*	1(af)
Osteomyelitis	9	7	3	1(af)	2	1(bl) + 1(af)		0	1 Sp	0
Pneumonia and/or pleurisy	50	11	1	1(bl)	5	3(pl) + 1(af)		0	5 Sp	1(bl) + 1(pl)
Shock	11	8	3	3(bl)	3	1(af)		0	1 *Staph. epid.* 1 Sp	0 1(pl)
Bacteraemia	34	31	11	9(bl)	12	9(bl) + 1(pl)	3	3(bl)	2 *Staph. epid.* 1 *E. coli* 2 Sp	1(bl) 0 1(bl) + 1(pl)

[a]Site of invasive infection: af, articular fluid; bl, blood; pl, pleura.
Staph. epid., *Staphylococcus epidermidis*; SA, *Staphylococcus aureus*; GABHS, group A β-haemolytic streptococci; Hi, *Haemophilus influenzae*; Sp, *Streptococcus pneumoniae*; MC, *Moraxella catarrhalis*.

superinfection associated with varicella in children, and both pathogens can be invasive [8,9]. A recent increase in the frequency of invasive group A β-haemolytic streptococcal infection in children has been reported in France, but the absence of previous data concerning varicella prevents comparison with increases reported previously in the USA [9–11] (http://www.invs.sante.fr/publications/2005/snmi/pdf/bacteriemies_meningites.pdf). *Strep. pneumoniae* was isolated mostly from patients with respiratory symptoms, which is consistent with the known epidemiology of pneumococcal infections among young children in France before the implementation of universal vaccination [12]. More surprising was the fact that *N. meningitidis* was the only pathogen identified in three patients with bacterial meningitis [13,14]. Case reports of a chronological relationship between invasive meningococcal disease and varicella have been published previously. Co-infection with varicella is possible, although initial varicella infection might have resulted in local mucosal lesions and immunosuppression, and thereby lowered the mucosal threshold for invasive bacterial superinfection.

Paediatric varicella represents an avoidable burden of hospitalisation and complications in France. Surveillance of varicella-associated complications is of interest and should be used to monitor the impact of varicella immunisation policies.

ACKNOWLEDGEMENTS

The authors express their grateful thanks to all the participants in the study. Financial support was provided by Laboratoire Sanofi Pasteur MSD, Groupe de Pathologie Infectieuse Pédiatrique de la Société Française de Pédiatrie (GPIP) and the Association Clinique et Thérapeutique Infantile du Val de Marne (ACTIV).

REFERENCES

1. Centers for Disease Control and Prevention. Epidemiology and prevention of vaccine-preventable diseases. In: Atkinson W, Hambursky J, McIntyre L, Wolfe S, eds, *The pink book*, 9th edn. Atlanta, Washington, DC: Public Health Foundation, 2006; 171–192.
2. Nguyen HQ, Jumaan AO, Seward JF. Decline in mortality due to varicella after implementation of varicella vaccination in the United States. *N Engl J Med* 2005; **352**: 450–458.
3. Anonymous. Calendrier vaccinal 2006 et autres avis du Conseil supérieur d'hygiène publique de France relatifs à la vaccination. *Bull Epidemiol Hebd* 2006; **29–30**: 211–226.
4. Bonmarin I, Ndiaye B, Seringe E, Levy-Bruhl D. The epidemiology of varicella in France. *Bull Epidemiol Hebd* 2005; **8**: 30–32.
5. Emery C, Lancon F, Fagnani F, Pechevis M, Durand I, Floret D. ENVOL study on the medical management of varicella and its complications in French ambulatory care. *Med Mal Infect* 2006; **36**: 92–98.
6. Dubos F, Grandbastien B, Hue V *et al.* Epidemiology of hospital admissions for paediatric varicella infections: a one-year prospective survey in the pre-vaccine era. *Epidemiol Infect* 2007; **135**: 131–138.
7. Mallet E, Maitre M, Delalande-Dutilleul L, Marguet C, Mouterde O. Evaluation of varicella complications through a retrospective hospital survey in a paediatric center over 16 years in France. *Arch Pediatr* 2004; **11**: 1145–1151.
8. Lesko SM, O'Brien KL, Schwartz B, Vezina R, Mitchell AA. Invasive group A streptococcal infection and nonsteroidal antiinflammatory drug use among children with primary varicella. *Pediatrics* 2001; **107**: 1108–1115.
9. Peterson CL, Mascola L, Chao SM *et al*. Children hospitalized for varicella: a prevaccine review. *J Pediatr* 1996; **129**: 529–536.
10. Cohen R, Aujard Y, Bidet P *et al. Streptococcus pyogenes*, an emerging pathogen. *Arch Pediatr* 2005; **12**: 1065–1067.
11. Doctor A, Harper MB, Fleisher GR. Group A beta-hemolytic streptococcal bacteremia: historical overview, changing incidence, and recent association with varicella. *Pediatrics* 1995; **96**: 428–433.
12. Gendrel D. Community-acquired pneumonia in children: etiology and treatment. *Arch Pediatr* 2002; **9**: 278–288.
13. Maitland K. Temporal association of chickenpox and meningococcal disease in children: a report of three cases. *Acta Paediatr* 2000; **89**: 744–745.
14. Travaglini M, Gubler J, Buhlmann U, Goetschel P. Varicella zoster virus infection complicated by *Neisseria meningitidis* bacteraemia in two children. *Eur J Pediatr* 2001; **160**: 399.